

WHAT IS CLAIMED IS:

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Sub 1
1. A delivery system for delivering genetic material to cardiac tissue, comprising:  
a supply of conduction protein genetic material;  
reservoir means for containing said conduction protein genetic material; and  
delivery means for delivering said conduction protein genetic material from said reservoir to said cardiac tissue so as to contact a plurality of cells in said cardiac tissue;  
wherein said delivery means comprises:  
a catheter with a distal end having an opening at said distal end;  
means for delivering said conduction protein genetic material from said reservoir through said opening;  
mapping electrode means positioned at said distal end of said catheter for carrying out mapping of said cardiac tissue; and  
conductor means for connecting said mapping electrode means to the proximal end of said catheter.
2. The delivery system of claim 1, wherein said delivery means comprises a catheter with a distal end having an opening at said distal end, said delivery means comprising means for delivering said genetic material from said reservoir through said opening, and further comprising:  
mapping electrode means positioned at said distal portion for carrying out mapping of the patient's heart so as to identify said cardiac location; and  
conductor means for connecting said mapping electrode means to the proximal end of said catheter.
3. The delivery system of claim 1, wherein said supply of genetic material comprises a bolus of conduction protein genetic material selected for the function of enhancing cardiac cell conductivity.

Sub D<sup>2</sup> 4. The delivery system of claim 1, wherein said delivery means comprises a catheter with a distal end portion, and said reservoir means is located in said distal end portion.

Sub C<sup>2</sup> 5. The delivery system of claim 4, wherein said distal end portion comprises a hollow helical element forming an interior, and said reservoir means comprises said interior with said supply of conduction protein genetic material therein.

6. A delivery system for delivering genetic material to cardiac tissue, comprising:  
a supply of conduction protein genetic material;  
reservoir means for containing said conduction protein genetic material; and  
delivery means for delivering said conduction protein genetic material from said reservoir to said cardiac tissue so as to contact a plurality of cells in said cardiac tissue;

wherein said delivery means comprises:

a catheter comprising a lumen for delivering said conduction protein genetic material therethrough, a distal tip communicating with said lumen for contacting said plurality of cells with said conduction protein genetic material, and a pacing electrode.

7. The delivery system of claim 6, wherein said distal tip is a hollow helical needle tip.

8. The delivery system of claim 6, wherein said catheter is a transvenous endocardial catheter.

9. The delivery system of claim 1, wherein said reservoir contains a supply of 0.1-10 ml of said genetic material.

Sub C<sup>2</sup> 10. A delivery system for delivering genetic material to cardiac tissue, comprising:

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a supply of conduction protein genetic material;  
reservoir means for containing said conduction protein genetic material; and  
delivery means for delivering said conduction protein genetic material from said  
reservoir to said cardiac tissue so as to contact a plurality of cells in said cardiac tissue;  
wherein said delivery means comprises:  
a catheter comprising a distal portion and distal tip, and wherein said  
reservoir means is contained in said distal portion;  
means for forcing said conduction protein genetic material from said  
reservoir means and out of said distal tip; and  
pacing electrode and conductor means for connecting said pacing  
electrode to the proximal end of said catheter.

11. The delivery system of claim 10, wherein said force means comprises a  
stylet.

12. The delivery system of claim 1, wherein said delivery system comprises a  
hollow helical screw-in element loaded with a bolus of said genetic material.

13. The delivery system of claim 12, wherein said element comprises ports for  
egress of said genetic material into said cardiac tissue when said element is <sup>s</sup>crewed into said  
tissue, and further comprising plugs in said ports to maintain them normally closed but which  
dissolve when said element is positioned within said cardiac tissue.

14. The delivery system of claim 1, wherein said genetic material is DNA or RNA.

15. The delivery system of claim 14, wherein said DNA or RNA encodes cardiac  
gap junction proteins.

16. ~~The delivery system of claim 15, wherein said cardiac gap junction proteins are connexin proteins selected from the group consisting of Cx40, Cx43, and Cx45.~~

17. ~~The delivery system of claim 1, wherein said genetic material is protein.~~

18. ~~The delivery system of claim 17, wherein said protein is cardiac gap junction protein.~~

19. ~~The delivery system of claim 18, wherein said cardiac gap junction proteins are connexin proteins selected from the group consisting of Cx40, Cx43, and Cx45.~~

20. An implantable delivery system for delivering doses of genetic material to cardiac tissue, comprising:

a supply of conduction protein genetic material;

a catheter, said catheter having a distal tip portion for engaging the cells of said cardiac tissue and delivering thereto said conduction protein genetic material;

reservoir means for holding said supply of conduction protein genetic material and providing it to said distal tip portion of said catheter; and

delivery means for delivering a therapeutically effective amount of said conduction protein genetic material from said reservoir means through said distal tip portion to said cardiac tissue;

wherein said delivery means comprises mapping electrode means or pacing electrode, and conductor means for connecting said mapping electrode means or pacing electrode to the proximal end of said catheter.

21. The system as described in claim 20, further comprising:

control means for controlling operation of said delivery means to deliver said doses.

22. The implantable delivery system of claim 21, wherein said control means comprises initiating means for initiating delivery of said genetic material, said initiating means comprising an external programmer.
23. The implantable delivery system of claim 21, wherein said control means comprises automatic means for automatically initiating delivery of said genetic material.
24. A combined mapping and delivery system for delivering genetic material to cardiac tissue comprising:  
a supply of conduction protein genetic material;  
reservoir means for containing said conduction protein genetic material;  
mapping means for mapping said cardiac tissue; and  
delivery means within said mapping means for delivering said conduction protein genetic material from said reservoir to said cardiac tissue so as to contact a plurality of cells in said cardiac tissue.
25. The combined mapping and delivery system of claim 24, wherein said mapping means comprises a catheter or peelable introducer sheath having two conductor means and said delivery means comprises a catheter having a distal end portion comprising a hollow helical element.
26. A method of treatment to improve the conductive properties of a localized area of a patient's heart, comprising:  
determining at least one localized area of said patient's heart which exhibits ineffective or harmful conductive properties;  
selecting a genetic material which improves the conductive properties of cardiac cells in and around said localized area; and

contacting said cardiac cells with a therapeutically effective amount of said genetic material, thereby improving the overall cardiac function of the patient's heart.

27. The method of claim 26, comprising selecting a genetic material having the property of enhancing conductivity, and contacting cardiac cells of said cardiac area with said genetic material.

28. The method of claim 26, comprising selecting a genetic material having the property of slowing conductivity, and contacting cells of said localized area with said selected genetic material.

29. The method of claim 28, comprising contacting cells in the patient's AV nodal tissue.

30. The method of claim 28, comprising contacting cells in the patient's His tissue and bundle branches.

31. The method of claim 26, comprising mapping said patient's heart to determine said localized area.

32. The method of claim 26, comprising selecting said predetermined genetic material from types of DNA and RNA which impart chronic change in conductive properties to said cardiac cells.

33. The method of claim 32, comprising selecting DNA or RNA of a type which encodes cardiac gap junction proteins.

34. The method of claim 33, comprising selecting connexin proteins from the group consisting of Cx40, Cx43, and Cx45.

35. The method of claim 26, comprising selecting protein of a form that imparts acute change in conductive properties to said cardiac cells.

36. The method of claim 35, comprising selecting a cardiac gap junction protein.

37. The method of claim 36, comprising selecting said cardiac gap junction protein from the group consisting of Cx40, Cx43, and Cx45.

38. The method of claim 26, comprising providing an endocardial catheter having a distal injection element, and wherein said contacting comprises positioning said injection element in an area adjacent to said localized area and releasing said genetic material-area through said injection element into said adjacent area.

39. The delivery system of claim 6, wherein said reservoir contains a supply of 0.1-10 ml of said genetic material.

40. The delivery system of claim 6, wherein said delivery system comprises a hollow helical screw-in element loaded with a bolus of said genetic material.

41. The delivery system of claim 40, wherein said element comprises ports for egress of said genetic material into said cardiac tissue when said element is screwed into said tissue, and further comprising soluble plugs in said ports to maintain them normally closed but which dissolve when said element is positioned within said cardiac tissue.

42. The delivery system of claim 6, wherein said genetic material is DNA or RNA.

43. The delivery system of claim 42, wherein said DNA or RNA encodes cardiac gap junction proteins.

44. The delivery system of claim 43, wherein said cardiac gap junction proteins are connexin proteins selected from the group consisting of Cx40, Cx43, and Cx45.

45. The delivery system of claim 6, wherein said genetic material is protein.

46. The delivery system of claim 45, wherein said protein is cardiac gap junction protein.

47. The delivery system of claim 46, wherein said cardiac gap junction proteins are connexin proteins selected from the group consisting of Cx40, Cx43, and Cx45.

48. The delivery system of claim 10, wherein said delivery system comprises a hollow helical screw-in element loaded with a bolus of said genetic material.

49. The delivery system of claim 48, wherein said element comprises ports for egress of said genetic material into said cardiac tissue when said element is screwed into said tissue, and further comprising soluble plugs in said ports to maintain them normally closed but which dissolve when said element is positioned within said cardiac tissue.

50. The delivery system of claim 10, wherein said genetic material is DNA or RNA.

51. The delivery system of claim 50, wherein said DNA or RNA encodes cardiac gap junction proteins.

52. The delivery system of claim 51, wherein said cardiac gap junction proteins are connexin proteins selected from the group consisting of Cx40, Cx43, and Cx45.

53. The delivery system of claim 10, wherein said genetic material is protein.



54. The delivery system of claim 53, wherein said protein is cardiac gap junction protein.

55. The delivery system of claim 54, wherein said cardiac gap junction proteins are connexin proteins selected from the group consisting of Cx40, Cx43, and Cx45.

56. A method of expressing conduction protein in cardiac tissue comprising delivering an expression vector comprising a nucleotide sequence encoding said conduction protein to said cardiac tissue using the delivery system of claim 1, 6, 10, 20 or 24.

57. The method of claim 56 wherein said conduction protein is selected from the group consisting of Cx40, Cx43, and Cx45.

58. The method of claim 57 wherein said expression vector comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, and SEQ ID NO:5.

59. The method of claim 56 wherein said expression vector is a viral vector.

60. The method of claim 59 wherein said viral vector is an adenoviral vector.

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